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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/717,450	11/20/2000	Lisa Ann Neuhold	0630/D532US1	5417

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EXAMINER

WILSON, MICHAEL C

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 06/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/717,450

Applicant(s)

NEUHOLD ET AL.

Examiner

Michael C. Wilson

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 April 2006.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 55-57, 59-68, 72-77 and 79-100 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 55-57, 59-64, 66-68, 72-77, 79 and 81-100 is/are rejected.
- 7) ☒ Claim(s) 65 and 80 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 4-10-06 & 7-28-03.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claims 58, 69-71 and 78 have been cancelled. Claims 55-57, 59-68, 72-77 and 79-100 remain pending and under consideration in the instant office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's arguments filed 4-10-06 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 112

Written description

1. Claims 55-57, 59-64, 66-68, 72-77, 79 and 81-100 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record.

The phrase "chondrocyte-specific promoter" as newly amended lacks written description because the specification does not disclose any promoters that meet the description of "chondrocyte-specific promoters" provided in the specification other than the type II collagen promoter.

The ordinary and customary meaning attributed to the phrase by those skilled in the art taken with the teachings in the specification is limited to a promoter that provides expression that is greater in chondrocytes than in other tissues. This interpretation of "chondrocyte-specific promoter" is broader than in the interpretation in the previous office action (sent 11-7-05) and is discussed briefly below.

The specification

Pg 16, lines 7-13, describes the function of the promoter as being "joint-specific" (the transcriptional activator polypeptide under the control of a joint-specific promoter...."

Pg 15, line 19, though pg 16, line 9, defines the function of "joint-specific promoters" ("Promoters that direct transcription selectively in joint tissues. Joint-specific expression as used herein refers to expression that is greater in joints than in other tissues; typically, the level of expression in non-joint tissues is less than 10% of the level of expression in joints. Preferably, expression in non-joint tissues is undetectable. Useful promoter sequences that confer joint-specific expression on a sequence to which they are operably linked to include without limitation sequences derived from the collagen type II promoter"). The specification only describes the structure of one promoter having the function defined in the specification. Describing the structure of one species within a genus defined by function is not adequate written description of other structures within the genus. Other promoters that are "joint-specific" as defined on pg 15, lines 19, through pg 16, line 9 may not exist.

Pg 6, lines 15-20, refers to "joint-specific promoters", specifically type II collagen promoter, but does not describe the structure of any other promoters having the same function.

Pg 36, lines 21, through pg 37, line 1, refers to a "joint-specific promoter (type II collagen", but does not describe the structure of any other promoters having the same function.

Pg 40, lines 1-22, Example 4 describes obtaining "joint specific expression conferred by type II collagen promoter" but does not describe any promoter other than type II collagen promoter having such function.

The art at the time of filing

Aggrecan

Pirok (J. Biol. Chem., 1997, Vol. 272, pg 11566-11574) who taught the chick aggrecan promoter. Pirok fails to indicate the chick aggrecan promoter provide greater expression in chondrocytes than in other tissues. The last line in the abstract of Pirok merely states the aggrecan regulatory region is important "in the tissue specific expression of the chick aggrecan gene." Pirok merely compared expression of the chick aggrecan promoter in chicken chondrocytes and fibroblasts in vitro; Pirok did not teach the aggrecan promoter provided greater expression in chondrocytes than in other tissues. Pirok taught the chick aggrecan promoter does not correlate to the mouse or rat promoter (pg 11567, 1st full ¶); therefore, one of skill would not necessarily expect the chick promoter to have the same specificity in a rat.

CD-RAP

Bosseroff of record taught the CD-RAP promoter and stated the "availability of a gene specific to chondrogenesis... provides a template for study of chondrocyte specific gene expression" (pg 520, last few lines of column 1). Bosseroff does not reasonably imply the CD-RAP promoter is chondrocyte-specific or provides expression in chondrocytes greater than in other tissues.

The Second Neuhold Declaration states the CD-RAP/MIA promoter may be substituted for the type II collagen promoter (¶ 7). Applicants' arguments were not found persuasive. The Second Neuhold Declaration does not teach the CD-RAP/MIA provides greater expression in chondrocytes than in other tissues. The Second Neuhold Declaration, ¶ 7, merely states the identity of other promoters within the genus "is not important." While the declaration states the CD-RAP/MIA promoter may be

substituted for the type II collagen promoter (§ 7), the declaration does not state the CD-RAP/MIA promoter provides greater expression in chondrocytes than in other tissues.

Others

Goldring of record taught collagen types II, IX, and XI and proteoglycan were chondrocyte-specific (abstract) but does not teach the collagen type IX, XI or proteoglycan promoters or that the promoters provide greater expression in chondrocytes than in other tissues.

The second Declaration by Askew discusses other references in paragraph 13 known in the art at the time of filing, but none of the references at the time of filing taught promoters that provide expression in chondrocytes greater than in other tissues.

Rejection

Given the ordinary and customary meaning attributed to the phrase by those skilled in the art taken with the teachings in the specification, the limitation of “chondrocyte-specific promoter” is limited to a promoter that provides expression that is greater in chondrocytes than in other tissues.

Defining the function of what applicants consider “joint-specific promoters” without describing the structure of adequate numbers of promoters having that function is simply a wish to identify promoters having that function. Defining the function of a promoter without describing the structure of a representative number of promoters having that function or comparing the structure of type II collagen promoter to other promoters, is not adequate description of “chondrocyte-specific promoters.”

Accordingly, describing a rat having a type II collagen promoter fails to describe the genus of rats having a “chondrocyte-specific promoter” as claimed. Adequate written description of a rat having a “chondrocyte-specific promoter” requires more than a mere statement that it is part of the invention. What is required is a description of a

reasonable number of rats having such promoters. Defining what applicants consider the function of a “chondrocyte-specific promoter” without describing the structure of promoters having that function is simply a wish to identify promoters having that function that can be used to make the rat claimed. Naming a promoter that may exist, in the absence of knowledge as to what that material consists of, is not a description of that material. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

Applicants provide the second Askew Declaration and argue other chondrocyte-specific promoters were known in the art at the time of filing. Bosseroff taught the CD-RAP promoter and stated the “availability of a gene specific to chondrogenesis... provides a template for study of chondrocyte specific gene expression” (pg 520, last few lines of column 1). Bosseroff does not reasonably imply the CD-RAP promoter is chondrocyte-specific or provides expression in chondrocytes greater than in other tissues. Goldring teaches collagen types II, IX, and XI and proteoglycan are chondrocyte-specific collagens but does not teach the promoters of the genes or that the promoters provide greater expression in chondrocytes than in other tissues. McDougall does not mention the link gene discussed in the Second Askew Declaration. Bosnakovski (2006) was not available at the time of filing, does not teach the sox9, aggrecan or COMP promoters, does not teach the sox9, aggrecan and COMP promoters provide expression in chondrocytes greater than in other tissues or that the sox9, aggrecan and COMP promoters were available at the time of filing.

Enablement

2. Claims 54-57, 59-64, 66-68, 72-77, 79 and 81-100 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a

transgenic rat or mouse whose genome comprises: a) a nucleotide sequence encoding a constitutively active, human MMP that cleaves Type II collagen, wherein the nucleotide sequence is operatively linked to a regulatable promoter; and b) a nucleotide sequence encoding a transcription activator or repressor protein operatively linked to a Type II collagen promoter, wherein expression of the metalloproteinase is capable of being repressed in the rat or mouse until adulthood, and wherein the metalloproteinase is capable of being expressed in the rat or mouse during adulthood to a level sufficient to cause degradation of type II collagen, does not reasonably provide enablement for any "chondrocyte-specific promoter". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for reasons of record.

THE CLAIMS

Claims 55-57, 59-64, 66-68, 72-77, 79 and 81-97 encompass transgenic rats made using a "chondrocyte-specific promoter" and methods related thereto. Claims 98-100 encompass methods of using a transgenic mouse having a "chondrocyte-specific promoter".

TEACHINGS IN THE SPECIFICATION AND CLAIM INTERPRETATION OF "CHONDROCYTE-SPECIFIC PROMOTER"

Pg 16, lines 7-13, describes the function of the promoter as being "joint-specific" (the transcriptional activator polypeptide under the control of a joint-specific promoter....")

Pg 15, line 19, though pg 16, line 9, defines the function of "joint-specific promoters" ("Promoters that direct transcription selectively in joint tissues. Joint-specific expression as used herein refers to expression that is greater in joints than in other

tissues; typically, the level of expression in non-joint tissues is less than 10% of the level of expression in joints. Preferably, expression in non-joint tissues is undetectable. Useful promoter sequences that confer joint-specific expression on a sequence to which they are operably linked to include without limitation sequences derived from the collagen type II promoter"). The specification only describes the structure of one promoter having the function defined in the specification. Describing the structure of one species within a genus defined by function is not adequate written description of other structures within the genus. Other promoters that meet the definition on pg 15, lines 19, through pg 16, line 9 may not exist.

Pg 6, lines 15-20, refers to "joint-specific promoters", specifically type II collagen promoter, but does not describe the structure of any other promoters having the same function.

Pg 36, lines 21, through pg 37, line 1, refers to a "joint-specific promoter (type II collagen", but does not describe the structure of any other promoters having the same function.

Pg 40, lines 1-22, Example 4 describes obtaining "joint specific expression conferred by type II collagen promoter" but does not describe any promoter other than type II collagen promoter having such function.

Given the teachings in the specification, the limitation of "chondrocyte-specific promoter" is limited to the definition of "joint-specific expression" on pg 15, line 19-20, i.e. expression that is greater in chondrocytes than in other tissues.

WORKING EXAMPLES

The specification explicitly teaches making a transgenic mouse whose genome comprises: a) a nucleotide sequence encoding a constitutively active, human MMP that cleaves Type II collagen, wherein the nucleotide sequence is operatively linked to a

regulatable promoter; and b) a nucleotide sequence encoding a transcription activator or repressor protein operatively linked to a Type II collagen promoter, wherein expression of the metalloproteinase is capable of being repressed in the mouse until adulthood, and wherein the metalloproteinase is capable of being expressed in the mouse during adulthood to a level sufficient to cause Type II collagen degradation in the joints of the mouse. Expression is controlled by the administration/withdrawal of tetracycline or other regulatory compound. The working examples are limited to the type II collagen promoter.

AMOUNT OF EXPERIMENTATION

While one of skill could determine whether a promoter provided greater expression in chondrocytes than in other tissues in a transgenic mouse or rat, no amount of experimentation would ensure that such a promoter existed. If no promoter greater expression in chondrocytes than in other tissues, any assay to determine whether a promoter provides such expression would be undue.

REJECTION OF "CHONDROCYTE-SPECIFIC PROMOTERS" - PROMOTERS THAT PROVIDE GREATER EXPRESSION IN CHONDROCYTES THAN IN OTHER TISSUES

The specification and the art do not teach the Type II collagen promoter or any other promoter causes expression greater in chondrocytes than other tissues. As such, a transgenic mouse or rat having a type II collagen promoter does not enable the genus of a transgenic mouse or rat having a "chondrocyte-specific promoter." Merely defining a "chondrocyte-specific promoter" without teaching any promoters that meet the definition is not an enabling disclosure.

ARGUMENTS

Applicants' arguments are essentially repeated from the written description rejection and are not persuasive for reasons set forth above.

Claim Rejections - 35 USC § 112 – indefiniteness

The rejection of claims 90-100 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been withdrawn in view of the amendment.

Art

The claims remain free of the prior art of record.

Claim Objection

Claims 65 and 80 remain objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on 571-272-0735.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

A handwritten signature in black ink, consisting of a series of vertical, wavy lines followed by a horizontal stroke that tapers off to the right.

MICHAEL WILSON
PRIMARY EXAMINER